ATTACHMENT C

NIH/NIDCR CONSENSUS DEVELOPMENT CONFERENCE (CDC) ON CARIES

SUBSECTION ON SALIVA AS A RISK FACTOR IN CARIES

EVIDENCE TABLE 1C.

AUTHOR	YEAR	CLINICAL EVIDENCE FOR THE PRESENCE/ABSENCE OF A PROTECTIVE EFFECT OF SALIVA AGAINST CARIES						
			Subject Demographics			Summary Information		
		Contributory Medical Condition	Age, Gender & Number	Source, Risk Definition and Other Data	Main Findings	Saliva-Caries Relationship	Authors' Conclusion	Comments/ Applicability of Findings
Almståhl et al.	1999	Primary Sjögren's syndrome (pSS) and Secondary Sjögren's syndrome (sSS)	10 subjects with pSS, 10 F, 0 M, mean age 56 ± 10 y, range 36-67 y; 10 subjects with sSS, 8 F, 2 M, mean age 60 ± 9 y, range 50-75 y; 10 controls for pSS, 10 F 0 M, mean age 54 ± 9 y, range 37-67 y; 10 controls for sSS, 8 F 2 M, mean age 57 ± 6 y, range 47-70 y	Sweden; The two control groups were also matched with respective SS groups for number of teeth	pSS patients had significantly lower flow rate (both stimulated and unstimulated) and higher filled surfaces (FS) vs. controls; sSS patients had significantly lower flow rate (both stimulated and unstimulated) but no difference in FS vs. controls; mean salivary pH and buffer capacity were within normal range in all subjects without significant difference; stimulated salivary flow rate for both SS groups was less than 1.0 ml/min whereas stimulated salivary flow rate was greater than 1.5 ml/min in both control groups	Yes	SS patients with low salivary flow rate may have increased risk of caries	Use of chewing gum and antiinflammatory drugs among some subjects may have confounded the results
Bergman and Ericson	1986	Subjects generally healthy	34 dental school patients were followed 3 years, mean age 61.7 y, age range 39-78, 16F, 18 M	Sweden; all subjects had received removable partial dentures	Salivary flow rate, buffer capacity and pH were not predictive of caries incidence either as single risk factors or when used in combination with other putative risk factors; when all examined risk factors were grouped together subjects with no negative risk factors had little caries, while subjects with high numbers of negative risk factors had a larger proportion of caries; 53% of the study subjects did not develop any carious lesions over the 3-year period; of 436 initially	No	No single caries risk factor seemed to be predictive of caries development;	The profile of combined risk factors (DFS, salivary, bacterial, oral hygiene) could predict caries incidence for the group but not for individual subjects

					intact surfaces, 31 (7.1%) were decayed or had been restored; of 422 initially restored surfaces, 26 (6.2%) exhibited recurrent caries			
Bhatia et al.	1986	Subjects generally healthy	20 children with no detectable caries (caries-negative), mean age 12.35 y, age range 10-14 y, 12F, 8M; 20 children with detectable caries (caries-positive), mean age 12.5 y, age range 10-14 y, 9F, 11M; 20 adults with no detectable caries (caries-negative), mean age 23.5 y, age range 20-25 y, 10F, 10M; 20 adults with caries (caries-positive), mean age 24 y, age range 20-25 y, 8F, 12M	India; Caries-negative children and adults both had DMFT=0; Caries positive children and adults both had DMFT=3	No statistically significant correlation was found between DMFT and total salivary IgA in either children or adults with caries; Mean total salivary IgA level was significantly higher ($p<0.01$) in caries-positive children compared with caries-negative children; No significant difference in mean total salivary IgA levels was found between caries-positive adults and caries-negative adults	No	These data do not support the hypothesis that the levels of salivary immunoglobulins necessarily correlate with the degree of immune protection against caries	Authors acknowledge that salivary titers of specific, rather than total, IgA may be a more useful parameter to be evaluated
Camling and Köhler	1987	Subjects generally healthy	Of 60 children from whom saliva samples were obtained, comparison was made between those designated caries experience-negative (n=22) and caries experience-positive (n=17), age range for both groups 37-72 months	Sweden; Subjects defined as: Caries experience-negative, dfs=0; Caries experience-positive, dfs>2	There was no significant difference in total IgA between children with and without caries experience; Of the various antigens tested, IgA antibody activity to Mutans streptococci antigen c and whole cells (serotype c) was higher in caries-negative children (31.5 ± 17.2 vs. 20.3 ± 12.3 and 18.6 ± 11.0 vs. 15.5 ± 14.3, expressed as per cent of a positive reference pool per mg total IgA); No significant differences were found in the level of any of the specific IgA antibodies in children with different levels of indigenous S. mutans	Possibly	This study offers no clear evidence for a protective role of salivary IgA antibodies against Mutans streptococci colonization	If one makes a distinction between initial colonization and subsequent caries infection, then the authors' conclusion relative to colonization appears justified; However, the authors' conclusion relative to caries protection is unclear
Chia et al.	1997	Subjects generally healthy	77 caries-active (CA) subjects, 80 caries-free (CF) subjects, age range of all subjects 18-20 y	Taiwan, Republic of China; Groups defined as CF, DMFS=0; CA, DMFS>1; In the CA group, DMFS ranged 1-36, mean 11.1 ± 7.2, median 13	Data indicate that levels of specific IgA antibodies to glucosyltransferases in whole saliva may be related to caries experience; CF subjects had significantly higher levels of antibodies to a 19 residue synthetic peptide homologous to amino acids 435-453 of Mutans streptococci glucosyltransferase (Gtf) and to GtfB/C or GtfC than CA subjects (2.52 ± 1.03, 1.92 ± 1.76, 1.46 ± 1.03 vs. 1.02 ± 1.21, 1.32 ± 0.61, 1.10 ± 0.51, respectively)	Yes	Data support the hypothesis that CF individuals have higher titers of antibody directed against glucosyltransferases	Regardless of the caries activity, antibodies against natural and synthetic glucosyltransferases were detectable in the saliva of all subjects; Unclear whether or not the levels of total IgA were the same in CA and CF groups

Collin et al.	1998	Non-insulin dependent diabetes mellitus (NIDDM)	25 NIDDM patients, 3F, 22 M, mean age 67 ± 5.5 y, age range 58-76 y (1 smoker); 40 non-diabetic controls, 19 F, 21 M, mean age 66 ± 5.1 y, age range 59-77 y (2 smokers)	Finland; mean age at diagnosis of diabetes 50 y (range 45-64 y); 55.7% NIDDM patients were dentate (mean 13.2 teeth); 52% control subjects were dentate (mean 15.1 teeth); risk defined as flow rate ≤ 0.8 ml/min for both groups	Significantly more males in NIDDM group (p=0.003); no significant differences between NIDDM and control groups for mean scores of DMFT, DS, DS (root), FS, FS (root); no significant difference between NIDDM and control groups for mean salivary flow rate (NIDDM = 1.5 ± 1.8 ml/min; control =1.3 ± 1.0 ml/min); salivary buffer capacity data not reported; NIDDM patients with flow rate ≥ 0.8 ml/min had increased caries prevalence (2.6 vs. 0.6 lesions; odds ratio 6.5; 95% CI 0.84-50.2); control subjects with flow rate ≥ 0.8 ml/min had decreased caries prevalence (0.8 vs.1.2 lesions; not significant)	Possibly	High salivary flow rate increased the risk of caries in NIDDM patients; caries protective effect of saliva observed in control subjects was lost in NIDDM patients	48% NIDDM patients were being treated with insulin; median glycosylated hemoglobin concentration (8.6%; range, 4.8-12.6%) indicated poor metabolic control of diabetes
Coogan and Motlekar	1996	ND/NA	30 subjects total, age range 12-20 y; 15 caries-free (CF); 15 caries-active (CA)	South Africa; Subjects consisted of urban Blacks from Soweto; Mean DMFT for CA=5.46 and CF=0	No significant difference in salivary flow rate was found between CA and CF groups; CA group consumed significantly more sucrose than CF subjects; CF group had higher salivary levels of acetic acid (p=0.05) than CA group	Possibly	In caries-free subjects the salivary acetic acid-acetate buffer system may protect against caries by counteracting the destructive effects of lactic acid	No data on actual pH measurements were provided; Role of acetic acid in caries is controversial
Dahllöf et al.	1989	Cleft lip/Cleft palate (CL/CP)	49 Cleft lip/Cleft palate (CL/CP) patients (No. CL ≅ CP); 21 F, 28 M, mean age 5.5 y; 49 age- and sex-matched controls	Sweden; CL/CP group was status post surgical; CL/CP divided into 2 subgroups based on involvement of alveolus (25 with, 24 without); no data on dysmorpholo-	Fluoride tablet use significantly more frequent in CL/CP group than control group; no significant difference in caries in CL/CP subgroups with or without involvement of the alveolus; nearly twice as many control children had no caries; caries prevalence significantly higher in CL/CP group; no significant differences between groups for incipient enamel lesions; CL/CP group had significantly lower flow rate (0.6 ± 0.4 vs. 0.8 ± 0.4, p< 0.01); CL/CP group had significantly more enamel hypomineralization	Yes	Children with CL/CP had significantly increased dfs than children without clefts; cleft type does not influence caries indices	The reason for significantly lower salivary flow rate in CL/CP children is unclear

				gic syndromic or genetic diagnosis				
Dahllöf et al.	1997	Various childhood cancers; Bone-marrow transplant (BMT)	26 BMT patients, divided into two subgroups: 14 children treated with combination of chemotherapy (CY) plus total body irradiation (TBI) 5 F, 9 M, mean age 8.0 ± 2.9 y, age range 5.4-12.0 y; 12 treated with CY only, 5 F, 7 M, mean age 8.2 ± 2.5 y, age range 4.0 – 11.6 y; 52 control children age- and sex-matched: 28 controls for TBI/CY group, 10 F,18 M, mean age 12.0 ± 2.3 y, age range 9.4 –16.0 y; 24 controls for CY only group, 10 F, 14 M, mean age 12.2 ± 2.4 y, age range 8.0 –15.6 y	Sweden; Article focus is pre-BMT conditioning regimen	Mean DFS increased during the 4-year observation period in both the BMT and control groups (including each subgroup); there was no significant difference in caries between TBI/CY and CY only groups; 4 years after BMT, CY group had a similar salivary flow rate as healthy control (1.3 ± 0.7 ml/min for both groups); the TBI/CY group had a significantly decreased flow rate (0.7 ± 0.5 ml/min) compared to the corresponding control group (1.6 ± 0.9 ml/min) (P<0.01); despite the significant difference in flow rate between TBI/CY and CY after 4 years, no significant correlation between caries and salivary flow rate was found; graft vs. host diseases (GVHT) did not appear to affect salivary flow rate; salivary flow rate in children increased with age	No	Prevalence of dental caries did not differ between children conditioned with total body irradiation or chemotherapy and healthy controls	Results may partly be due to the increased salivary flow rate which occurs with age in children; permanent salivary dysfunction was apparent in the TBI/CY group
Demers et al.	1992	Subjects generally healthy	302 children examined twice at a one-year interval, mean age 5.7 y ± 0.3 y	Canada; Children were divided into two groups: the caries-increment group and the no caries-increment group	Buffer capacity of stimulated whole saliva was not significantly different between the caries-increment group and the no caries-increment group (p=0.83); Buffer capacity failed to be a predictor for 1-year caries increment (odds ratio 1.0; 0.6-1.6 caries increment); Buffer capacity had a sensitivity of 32.4 and specificity of 67.3);143 children developed new caries over the study period; the mean increment for the whole group was 2.1 dmfs; the best predictors were caries experience and lactobacilli counts	No	Among all the factors evaluated, only caries experience and lactobacilli counts were very good at predicting caries increment over one year	It is unknown from this study if the buffer capacity of unstimulated whole saliva, rather than that of the evaluated stimulated whole saliva, would have had any predictive value
Dens et al.	1995	Various childhood cancers	52 children who had received cancer chemotherapy and had been in remission, age range 2-17 y; 63 healthy matched controls	Belgium; Cancer subjects were in event-free remission between 6 months and 10 years (median 4.1y);	Concentrations of total salivary IgA and IgG were within normal limits in both groups as well as in age subgroups within the test and control groups; No significant correlation was found between salivary IgA and caries prevalence in either group when compared as a whole; When compared by age subgroups, a negative correlation between sIgA and caries was observed in all age groups but this was only significant in the oldest subjects	Possibly	Salivary IgA and IgG return to normal by 6 months after chemotherapy; IgA may play a role in caries development	Cancer patients were treated with chemotherapy only; No subjects received head and neck radiation

				Cancer patients did not receive any special prophylactic treatment	(age 14-17 years)			
Dens et al.	1996	Various types of non-squamous cell cancers (leukemia, lymphoma, sarcoma)	52 children in cancer remission; age range, 2-17 y; a subgroup of cancer patients consisted of children diagnosed a maximum of 2 years before examination (mean age 6.9 y); 60 control children, age-, race- and social class-matched	Belgium; remission range 1- >11y; all cancers were blood and connective tissue types; no patients received regional or total body irradiation	No relationship was found between buffer capacity and caries prevalence; buffer capacity did not differ among the groups;	No	Previous cancer treatment in these long-term, event-free pediatric patients does not seem to have long-term effect on salivary buffer capacity	Patients were not irradiated but were treated with chemotherapy only; It is possible that inter-individual differences are due to various caries risk factors rather than long-term effect of cancer treatment
Dodds et al.	1997	Subjects generally healthy	85 subjects 18- 30 years of age; 49 caries active (CA) mean age 24.4 ±0.6 y; 20 male, 29 female; 38 caries free (CF) mean age 23.3 ±0.6 y, 19 male, 19 female; Totals for entire study were 39 men; 48 women; 44 non-hispanic white; 34 Mexican Americans; 6 Other	United States; CA (caries active) at least 5 surfaces requiring restorations CF (caries free) DMFS=0	Among all salivary parameters tested only K and Cl were slightly higher in CA group; All other parameters showed no differences between CA and CF groups	No	Women showed higher buffer capacity and higher protein concentrations but no differences with respect to caries	Weak positive correlation between caries activity and K and Cl concentrations in stimulated parotid secretions; Inconsistencies in numbers of subjects in various categories (i.e., 87 vs. 85 subjects total)
Drake et al.	1994	Subjects generally healthy; Medication use	611 total subjects over age 65 y examined at 18-month follow-up; 325 blacks, 280 whites, 6 other races.	United States; Slightly more blacks than whites were included in final follow-up sample	In bivariate correlations, the incidence of coronal caries in black subjects was inversely associated with use of antihistamines (Pearson's r= -0.11, p=0.0388) and self-reported dry mouth (Pearson's r= -0.12, p=0.0273); No such correlations were found for white subjects; In multivariate logistic regression, the incidence of coronal caries in white subjects was significantly associated with use of antihistamines (p=0.001); No such association was found for black subjects	Possibly	Several factors can contribute to the development of caries in both blacks and whites	Authors acknowledge that there may be other factors not sufficiently measured (e.g., immune response); It is interesting to note that the logistic models for blacks and whites were different from each other and that no variables were common to both models

Duggal et al.	1991	ND/NA	Age group 4-7 y: n=134 Age group 12-16 y: n=138	Northern India; 272 children	Inverse relationship of salivary Cu and F to dental caries in both 4-7 and 12-16 y age groups; no consistent relationship between Zn, Fe, Mn and caries.	Yes	Inverse relationship of Cu and F with caries status	Minimal details on caries assessment; No data on flow rates
Faine et al.	1992	Subjects generally healthy	20 subjects in root caries group, mean age 62 ± 9 y, 10 F, 10 M; 20 control subjects, mean age 62 ± 9 y, 10 F, 10 M	United States; of the 20 control subjects, 16 had no root caries and 4 had no root restorations placed within 5 y	Significant differences were found between root caries and control groups in the number of root caries (9.4 DFS vs. 0.7 DFS, respectively) and buffering capacity (final pH 5.3 ± 0.1 vs. final pH 6.3 ± 0.1, respectively); No differences were found in salivary flow rate between root caries group and control groups (1.4 ± 0.2 vs. 1.7 ± 0.2 ml/min, respectively)	Possibly	Subjects with root caries had significantly lower buffering capacity but similar salivary flow rates when compared to root caries-free controls	Although buffering capacity was lower in the root caries group, both groups had buffering capacities that could be considered to be within normal limits
Fiehn et al.	1986	Subjects generally healthy	38 young adults subdivided into three groups; Caries-inactive group (CI), 13 subjects, 7 F, 6 M, age range 20-30 y; Low caries-active group (LCA), 14 subjects, 6 F, 8 M, age range 20-30 y; Moderate-high caries-active group (HCA), 11 subjects, 6 F, 5 M, age range 20-30 y	Denmark; Definition of caries groups: CI, no carious lesions, DMFS<20; LCA,, 1-2 carious lesions, DMFS 20-35; HCA, >2 carious lesions, DMFS > 35	No significant difference was observed between the CI and HCA groups for salivary α-amylase and sucrase activity	No	Results show that laboratory tests are unreliable indicators of caries risk in young adults	Authors acknowledge that the negative results may reflect the multifactorial nature of caries and/or insufficiency of the laboratory methods used
Franco et al.	1996	Severe congenital cardiac disease	60 treated pediatric cardiology patients, mean age 8.9 ± 3.9 y; 60 healthy matched control subjects, mean age 8.8 ± 4.0 y	England; Study group had a wide range of cardiac problems	There was no significant difference between cardiac and control groups for caries of either primary or permanent teeth: dmft and DMFT of the two groups were similar (3.9 and 2.7 vs. 3.7 and 2.0, respectively); Number of untreated carious lesions was higher in the cardiac group (52% vs. 32%); There was no significant difference in salivary IgA level between cardiac and control groups	No	Children with severe cardiac disease have significantly higher levels of untreated disease making them more susceptible to further cardiac injury	The lack of difference in caries status between the 2 groups renders the salivary IgA comparison inconclusive; Cardiac group had a higher number of subjects who had never been to the dentist (19% vs. 5%)
Fure	1998	Subjects generally healthy	148 aged patients, 69 F, 79 M; divided into 3 age groups: 60-year-olds, 69 subjects (28 F, 41 M); 70-year-olds, 51 subjects (24 F, 27 M); 80-year-olds, 28	Sweden	In stepwise regression analysis salivary flow rate and buffer capacity were not strong predictors of the incidence of coronal or root caries; 73% of the participants developed carious lesions during the 5-year study; incidence of coronal and root caries increased with age; 18% had unstimulated salivary flow < 0.1ml/min; 14% had stimulated	No	With increasing age salivary flow rate decreases while bacterial counts increase,	Nearly half the subjects were taking drugs which could have xerostomic side effects, possibly confounding the data

			subjects (17 F, 11 M)		salivary flow < 0.7 ml/min with a mean rate of 2.0, 1.6 and 1.3 for the 60-y, 70-y and 80-y groups, respectively; Mean salivary buffer capacity significantly increased over 5 years		indicating that there is an increased risk of dental caries with age owing to unfavorable microbial and salivary conditions	
Furhoff et al.	1998	Medical symptoms possibly related to side effects of mercury in dental fillings	67 patients, age 49±12 y, 49 F, 18M; 64 controls, age 49± 12 y, 48F, 16M	Sweden	A significant relationship ($p<0.05$) was found between low unstimulated saliva secretion rate (0.1 ml/min) and untreated decayed surfaces, for both groups; No differences were found between DMFS and stimulated saliva flow rate	Yes	Patients' feelings of ill-health were more likely related to psychiatric than somatic diagnosis	Authors make a distinction between the protective effect of unstimulated vs. stimulated whole saliva
Gavaldá et al.	1999	Chronic renal failure (CRF)	105 CRF patients, 52F, 53M, mean age 58.9± 14.9 y; 53 healthy control subjects, 24F, 29M, mean age 55.7±10.7 y	Spain; subjects were receiving hemodialysis (HD) 59.8±43.9 months, range 1-104 months	Stimulated salivary secretion rate was significantly lower in CRF patients than in controls for both whole saliva($t=-5.2$; $P<0.001$) and parotid saliva ($t=-2.6$; $P=0.01$); Unstimulated whole saliva secretion rates were not different between CRF and control groups; Regardless of the differences in the salivary parameters, the CAO index was not significantly higher among CRF patients than controls (14.9±8.7 vs. 13.3 ±7.9, respectively; $t=1.1$, $P=0.3$)	No	There is significantly lower salivary secretion among CRF patients than in healthy controls which might be attributable to altered gland function and/or a restriction in fluid intake among these patients	The lowered salivary flow rates seen in the CRF patients might be considered to be at the low end of normal range
Gregory et al.	1986	Subjects generally healthy	3 groups, 11 subjects caries-free (CF), 4 F, 7 M, age range 18-60 y; 9 subjects low-caries susceptible (LCS), 3 F, 6 M, age range 22-40 y; 24 subjects high-caries (HCS) susceptible, 11 F, 13 m, age range 19-44 y	United States; Caries-free group had no detectable DMFS; Low caries-susceptible group had DMFS score <3 and two or fewer small, unfilled lesions not extending into the dentin; High caries-susceptible	An inverse relationship was observed between caries prevalence and levels of salivary anti-S. mutans IgA (mean ELISA units/ml: 96.2 CF group; 80.7 LCS; 39.2 HCS; $p<0.001$ for CF and LCS vs. HCS); The LCS group had significantly lower ($p<0.001$) DMFS and unfilled lesions than the HCS group	Yes	Naturally occurring salivary antibodies correlate with susceptibility to dental caries	The range of salivary IgA levels showed considerable overlap among the 3 groups

				group had DMFS score > 10 and had 5 relatively large, unfilled, smooth surface lesions with at least one extending into the dentin				
Gregory et al.	1990	Subjects generally healthy	72 caries resistant (CR) subjects, 37 F, 35 M, age range 17-42 y; 59 caries-susceptible (CS) subjects, 30 F, 29 M, age range 19-44 y	United States; CR has DMFS score < 3; CS has DMFS score > 10 and at least 5 relatively large unfilled, smooth, surface lesions	In general the levels of salivary anti-S. mutans IgA were significantly higher in CR than in CS subjects; No significant differences in total parotid salivary IgA concentration were found between the two groups, however, CR subjects had significantly higher levels of total parotid salivary IgA2 but not IgA1 than CS subjects; CR and CS subjects had similar levels of lysozyme and lactoferrin in parotid saliva; CR subjects had lower S. mutans titers than CS subjects	Yes	Neutralization of S. mutans enzymes and inhibition of S. mutans virulence factors by saliva may be responsible for the lower numbers of carious lesions in CR subjects.	These data support the belief that salivary immune factors may limit the susceptibility to caries
Gregory et al.	1991	Smokeless tobacco use	32 smokeless tobacco users, 0 F, 32 M; age range 17-37 y; 33 non-tobacco controls, 0 F, 33 M; age range 18-37 y	United States; Tobacco use greater than 3 times a day for at least 3 years; Non-tobacco controls never used tobacco in any form	Smokeless tobacco users and non-tobacco using controls had similar levels of DMFS; flow rate of parotid and whole saliva were significantly lower in the smokeless tobacco users than in the controls; there were significantly higher concentrations of whole salivary IgA, IgA2 (but not IgA1) and J-chain in users than in control; whole saliva lysozyme and lactoferrin were significantly lower in users than in controls; immunoglobulin levels from parotid saliva show similar results as whole saliva	No	The differences in mucosal immune factors between users and controls may not be critical in the regulation of dental cares	Data do not support an important role for IgA against caries; No data represented on whether duration of tobacco use confounded the results
Gregory et al.	1995	Subjects generally healthy	20 caries-resistant (CR) subjects and 20 caries-susceptible (CS) subjects; sex, age and race distribution of CR and CS were similar	United States; Caries-resistant defined as free of caries; Caries-susceptible subjects defined as DMFS score > 10 and had 3 or more active lesions	Saliva from CR subjects had significantly higher ($p \leq 0.05$) levels of anti-S. mutans IgA antibody activity than saliva from CS subjects; CS patients have significantly higher numbers of S. mutans in whole saliva than CR subjects	Yes	Differences were found in salivary antibody reactivity between CR and CS subjects	Data suggest that the specific immune response in saliva may be an important factor in determining caries risk

Grindefjord et al.	1995	Subjects generally healthy	692 children, 344 F, 348 M, mean age 30 ± 3 months at initial examination (i.e., 2.5 year time point in the longitudinal study) and 42 ± 4 months at follow-up one year later	Sweden; 56% of the children were classified as having an immigrant background	Salivary buffer capacity had no significant relationship between children remaining caries free and children developing caries over one year; 92% of children with caries at initial examination developed new carious lesions during the 1-year period compared to 29% of the children who were caries-free at baseline (p<0.001)	No	Children with early caries development exhibit high caries progression as well as a high risk for further development of an extensive number of new carious lesions	Pre-existing caries appeared to be the best predictor of caries incidence; Children with immigrant background appeared to be at higher risk for the incidence of caries
Guivante-Nabet et al.	1999	Hospitalized geriatric patients with various systemic conditions	117 elderly patients were examined at baseline; 50 long-term care facility patients (LTCF) and 67 rehabilitation facility patients (RF); mean age 83.0 y, age range 64-102 y; In the present study only 32 of the 50 LTCF patients were re-examined 15 months later	France; Among the subjects with multiple systemic conditions (85.5% of the population), the number of diseases ranged from 2-8.	Salivary flow rate was inversely related to crown caries; Buffer capacity was inversely related to root caries; During the 15-month follow-up, the mean number of active root surfaces was significantly increased from 0.148 ±0.116 at baseline vs. 0.25±0.174 at the second examination	Possibly	Strongest relationship found was the negative relationship between buffer capacity and active root caries	Data presented is mostly cross-sectional given the relatively limited number of subjects available at follow-up
Hallett et al.	1995	Salivary duct surgery (sialodochoplasty); Cerebral palsy (CP)	19 CP patients treated with sialodochoplasty, 7 F, 12 M, mean age 6.2 ± 4.7 y; 75 CP patients treated nonsurgically, 29 F, 46 M, mean age 11.6 ± 3.7 y	Australia	The surgical group had significantly (p< 0.0001) more dental caries compared with control group (median DMFT=5.0 vs. 0.0, respectively) but had no difference in salivary buffer capacity	No	Although no caries predictors were identified, alterations to the caries protective role of saliva are considered the likely cause of the difference between the two groups	The authors expected difference in saliva buffer capacity was not observed; Flow rate measurement was not attempted due to its difficulty in these patients; Initial assumption of altered buffer capacity is equivocal
Hellyer et al.	1989	ND/NA	146 subjects, 97 F, 49M, mean age 69.3 y	United Kingdom; Mean number of teeth 20.2; 57.8% of subjects wore dentures	The number of root carious lesions was not negatively correlated with salivary flow rate or buffering capacity; Mean number of root carious lesions was 2.18±2.04, males had more lesions than females (3.00±1.98 and 1.76±1.96, respectively); Individuals not wearing dentures had significantly fewer root lesions than denture wearers (1.40± 1.59 and 2.77 ± 2.15, respectively)	No	Root caries prevalence was significantly correlated with denture wearing, age, salivary counts of mutans streptococci, lactobacilli, and yeasts	The authors acknowledge that the predictive ability of these tests remains to be determined

Hocini et al.	1993	ND/NA	21 caries-susceptible (CS) subjects, 10F, 11 M, age range 20-63 y; 22 caries-resistant (CR) subjects, 9F, 13M, age range 22-64 y	France; DMFT values were CR<2 and CS>10	No significant quantitative differences in total IgA and no significant qualitative differences in specific IgA antibodies were observed between CR and CS groups; Whole saliva flow rates were not significantly increased in the CR group in comparison with that of the CS group; Lactoferrin level and secretion rate were higher in the CR group but without statistical significance	No	Naturally induced sIgA antibodies against S sanguis, S. sobrinus, and the major antigens of the latter are not sufficient to inhibit caries development.	Data do not support a caries-protective role for salivary IgA
Holbrook	1993	Subjects generally healthy	158 children, 90F, 68M, initially 4-years-old, followed longitudinally for 2 years; 128 children were reexamined at age 5 y, 110 children were re-examined at age 6 y	Iceland	Low salivary flow rate and pH were significantly associated with high caries scores ($p<0.05$); Higher caries scores were found in children with a low buffer capacity but this was not statistically significant	Yes	Children with the lowest salivary flow rate and pH were unlikely to be caries-free	There was an uneven distribution of caries in pre-school children in the Reykjavik population
Holbrook et al.	1993	Subjects generally healthy	158 children, 90F, 68M, initially 4-years-old, followed longitudinally for 2 years; 128 children were reexamined at age 5 y, 110 children were re-examined at age 6 y	Iceland; Risk defined as: $\geq$3 new carious lesions, S. mutans count $\geq 10^5$ cfu/ml, lactobacilli count $\geq 10^4$ cfu/ml, ph <7, stimulated flow rate < 1 ml/min, buffer capacity < pH 5.5	Caries incidence was significantly associated with some salivary variables in direct correlations, but appeared less associated with salivary variables when data were examined by stepwise regression analysis; Odds ratios for dmfs at age 6 years old were: 2.07 for low (<pH 7) salivary pH ($p< -0.001$); and 1.31 for low (<1 ml/min) stimulated salivary flow ($p< -0.5$, NS); Low buffer capacity had sensitivity=0.23, specificity=0.81; Low salivary flow rate had sensitivity=0.21, specificity=0.78; Positive and negative predictive values of salivary parameters ranged approx. 0.4-0.6	Yes	This study confirms the relationship between caries incidence and low salivary flow rate and pH	It appears from this study that salivary flow rate, pH, and buffer capacity collectively are modest predictors having good specificity but poor sensitivity
Johansson et al.	1992	Chronic malnutrition (protein-energy malnutrition; PEM)	34 Indian children with moderate-to-severe PEM; 34 Indian age- and sex-matched healthy children (normal weight-for-age) or children with mild PEM; 33 age- and sex-matched healthy Swedish children (for saliva comparisons); age range for all groups 8-12 y	India; Sweden; Severe, moderate and mild PEM patients and normal subjects were determined based on weight-for-age or height-for-age ratio	Moderate/severe PEM group had significantly higher dmfs and ds (but not DMFS and DS) than the mild/normal PEM group when compared by weight-for-age; Moderate/severe PEM group had significantly higher ds, DMFS and DS (but not dmfs) than the mild/normal PEM group when compared by height-for-age; Well-nourished Swedish children had a significantly higher secretion rate ($p< 0.05$) than the age- and sex-matched mild/normal PEM Indian group; Severely malnourished children had a significantly lower buffer capacity than the mild/normal PEM group; however, the well-nourished Swedish children had a markedly lower buffer capacity than all Indian children	Possibly	Chronic malnutrition reduced the secretion rate of stimulated but not unstimulated saliva; Salivary buffer capacity decreased linearly with decreased salivary secretion rate	Comparisons among the groups were influenced by the criteria used to define malnutrition; Some differences in apparent caries susceptibility were seen between primary and permanent teeth; Chronic malnutrition may increase caries risk due to changes in salivary flow

Kirstilä et al.	1994	Common variable immunodeficiency (CVI)	15 CVI patients, 6F, 9M, age range 7-67 y; all patients were on Ig-replacement therapy (median duration 10 y; range 2-25 y); The Ig-replacement therapy had normalized IgG but not IgA or IgM levels in both serum and saliva; 15 controls, 6F, 9M, age range 7-63 y	Finland; No. of antimicrobial therapy episodes during the preceding year was 3.3±2.1 for CVI group and 0.7± 0.8 for control group; All subjects showed no signs of infection	No major differences were found between the immunodeficient patients and the controls in DMFT/dmft, DMFS/dmfs, salivary flow rate and the innate, nonimmune salivary defense factors (except for slightly increased total salivary peroxidase in the CVI group)	No	The results showed no notable differences between the 2 groups with respect to dental caries and innate, nonimmune salivary defense factors, suggesting the existence of a "backup system"	In immunodeficient patients the salivary nonimmune defense system may compensate for diminished salivary immune defense factors; Immunodeficient patients with normal salivary flow rate appear to have caries risk no different from immunocompetent individuals
Kirstilä et al.	1998	Subjects generally healthy	63 subjects, 30F, 33M, mean age at baseline was 12.5 y	Finland	On the basis of baseline data it appears that the two-year caries incidence was inversely related with total IgG and hypothiocyanite, and directly related with anti-S. mutans IgG; Statistically significant increases in salivary flow rate ($p<0.001$) and agglutination activity ($p<0.001$) were observed as well as significant decreases in salivary concentration of lactoferrin ($p<0.0001$) and lysozyme ($p=0.001$); No significant long-term changes in total salivary IgA antibodies were detected but anti-S. mutans IgA increased significantly ($P=0.006$)	Possibly	None of the single salivary antimicrobial factors has sufficiently strong power to have diagnostic significance in vivo with respect to caries incidence	Data presented are difficult to interpret due to the low caries incidence found in the study group, Less than 25% children developed new caries, with low DMFT and DMFS (both <1.0)
Laurikainen and Kuusisto	1998	Asthma	37 asthmatics patients, of these 33 were included, 24 F 9M; mean age 36.0 ± 7.4 y; 35 non-asthmatics controls, mean age 36.5 ± 7.1 y	Finland; mean duration of asthma 5 years (range ≤ 1-24 years)	DMFT and pH in both groups were not significantly different	No	Data support a higher risk of periodontal disease, mucosal lesions and possibly caries in asthmatics	Flow rates for both groups were normal despite significant differences between them; data from the study do not support higher risk of caries in asthmatics
Lenander-Lumikari et al.	1998	Asthma	26 asthmatics patients, 21 F 5M; mean age 35.4 ± 7.3 y; 33 non-asthmatics controls, 23 F 10 M; mean age 36.5 ± 7.1 y	Finland	No difference in DMFT was seen between both groups; mean stimulated flow rate ($p\leq0.05$; 95% CI -0.57- -0.05) was lower in the asthmatics group compared with control; myeloperoxidase concentration was higher in asthmatics ($p\leq0.05$; 95% CI 4.4 -134.0); no differences were found for the other salivary factors between groups	No	Stimulated salivary flow rate decreases while myeloperoxidase concentration increases in adult asthmatics patients compared with controls	Unclear whether some subjects were the same as in the Laurikainen and Kuusisto (1998) study

Lowe et al.	1997	Subjects generally healthy	59 children age 12 years-old; 31 black and 28 white; no data on gender distribution	South Africa: approx. half the children were defined: as caries-free (DMFT=0) and half as caries-prone (DMFT≥ 3); caries-free and caries-prone groups consisted of approx. half black and white children	No significant differences in salivary glucose clearance rates were seen between caries free (DMFT=0) and caries active (DMFT≥3) children; Salivary glucose clearance rate was nearly double in black children compared to white children	No	Salivary glucose clearance is not suitable as a single caries risk factor	The portable glucometer used in this study was found to be useful for field studies
Lundgren et al.	1997	Range of medical status in very elderly subjects; Medication use (cardiovascular and psychoactive drugs)	92 patients, 52F, 40M, age 88 y were examined at baseline; At 4-year follow-up, 24 original patients were re-examined, age 92 y, 12F, 12M; At 4-year follow-up, 16 new patients were also examined, age 92 y, 11F, 5M	Sweden	Nine of the 24 longitudinally followed subjects had lost 1-5 teeth over 4 y, and 17 subjects had developed new caries (DFS); Mean caries increment over 4 years was 1.3 coronal and 3.6 root surfaces, and new DFS per 100 surfaces at risk was 4.3 coronal and 17.5 root surfaces; Significant differences in plaque score ($p<0.05$) and final pH of buffer capacity ($p<0.01$) were found, whereas saliva flow, independent of gender, was unchanged; Levels of lactobacilli and mutans streptococci were higher at 92 y but the differences between the age groups were significant only for lactobacilli; When subjects were dichotomized into 2 groups (DMFS≤2 and DMFS≥3), no significant differences were observed for salivary secretion rate, buffer capacity and sugar clearance time	No	Deteriorated dental status was commoner in those who used cardiovascular agents and/or psychoactive drugs than in those who did not.	Despite the use of potential xerostomia-inducing drugs, salivary flow rate remained within normal limits
MacEntee et al.	1993	Geriatric patients with a range of systemic conditions	156 elderly subjects (>65 y); 25% < 75 y, 50% 75-84 y, 25% >84 y; 117 F, 39 M; 63% lived in long-term care (LTC) facilities, 37% lived independently.	Canada	No differences were reported in stimulated whole saliva flow rates between the institutionalized and non-institutionalized subjects; Stimulated whole saliva flow rate was not significantly associated with caries increment in either the institutionalized or non-institutionalized subjects; Institutionalized subjects had more carious surfaces (7.4 vs. 1.5) and fewer restorations (29.7 vs. 51.6) than independently-living subjects at baseline; At the end of one year, 71% of institutionalized and 59% of independently-living subjects had at least one new carious lesion, the mean net DFS increment per subject was 4.6 and 2.0, respectively	No	Multivariate models identified caries at baseline, residence in long-term care facilities, high Lactobacilli counts, poor oral hygiene and frequent sugar consumption as risk factors for caries	It is unknown if evaluation of unstimulated whole saliva flow rates would have given different results; Residents of the long-term care facilities had severe functional disabilities and required substantial assistance with daily activities

Meurman et al.	1997	Lymphoma	Initially 79 treated lymphoma patients were evaluated (i.e., at baseline examination 5 y earlier), subjects were gradually lost over time; In the present study 22 survivors were evaluated at multiple time points over 5 years; 7F, 15M, mean age 49 y, age range 34-74 y; Comparison also made with data from 17 deceased subjects, mean age 52 y, age range 30-81 y, 7F, 10M	Finland; All patients were treated with combination chemotherapy for lymphoma	No difference was observed in caries rate between the survivors (DMF 22.6) and the deceased (DMF 20.6); Salivary flow rate was not affected by chemotherapy treatment (baseline 1.5 ± 0.7 ml/min for survivors and 1.5 ± 0.8 ml/min for deceased; 12 month follow-up, 1.2 ± 0.6 ml/min for survivors and 0.9 ± 0.6 ml/min for deceased), Salivary buffering capacity in survivors was higher than in deceased group (considered low in 32% vs. 69% subjects, respectively)	No	Salivary flow rate was not affected by the chemotherapy treatment; Low salivary buffering capacity may be linked with poor medical prognosis	No subjects received head and neck radiation; Buffering capacity was lower at the start of the treatment in the deceased group
Milosevic and Slade	1989	Anorexia nervosa; Bulimia nervosa	4 groups of individuals were evaluated: group 1 = bulimia with self-induced vomiting (SIV), 32 F, 1 M, mean age 25.0 ± 4.9y, age range 19-43 y; group 2 = bulimia w/o SIV, 7 F, 0 M, mean age 24.7 ± 6.8 y, age range 20- 36 y; group 3 = anorexia, 17 F, 1 M, mean age 23.6 ± 5.9 y, age range 16-36 y; group 4= controls, 50 F, 0 M, mean age 23.1 ± 4.9 y, age range 15-39 y	England	DMFS between the 3 eating disorder groups and controls were not different; Salivary buffer capacity did not differ among the 4 groups	No	Salivary buffer capacity in anorexics and bulimics is good	Presumably electrolyte balance was good in the vomiting subgroup
Najera et al.	1997	Sjögren's syndrome (SS)	25 SS (23 primary SS, 2 secondary SS) subjects, mean age 60.9 ± 13.5 y, age range 28-80 y, 23F, 2M; 24 healthy controls, mean age 58.3 ± 12.1 y, age range 30-77y, 22F, 2M	United States; Mean duration of SS symptoms 7.8 y; Mean duration since SS diagnosis 3.2 y; SS subjects all had dry mouth, dry eyes, at least one positive serum antibody (antinuclear	SS patients had significantly lower flow rates (0.17 ± 0.12 vs. 0.42 ± 0.14 ml/min/gland) and significantly higher DMFS scores (73.60 ± 34.57 vs. 52.50 ± 28.29) than healthy controls; No significant difference was found in mean salivary pH between the 2 groups	Yes	SS patients have a reduced salivary output and are at a higher risk for tooth decay compared with healthy controls	The increased DMFS scores in SS group appeared to be due to M and F components, rather than D component, because most SS patients did not have active carious lesions

				antibody, rheumatoid factor, SS-A, SS-B), and/or a positive labial minor salivary gland biopsy (focus score ≥1)				
Närhi et al.	1996	Non-insulin-dependent diabetes mellitus (NIDDM); Cardiovascular disease (CVD)	12 NIDDM subjects, mean age 79.8 ± 4.3 y, 5F, 7M; 20 NIDDM+CVD subjects, mean age 80.5 ± 4.6 y, 16F, 4M; 32 age-and sex-matched healthy controls, mean age 78.5 ± 3.6 y, 21F, 11M	Finland; No study subjects had insulin-dependent diabetes mellitus	There were no statistically significant differences in unstimulated or stimulated salivary flow rates, salivary buffer capacity and caries prevalence among the 3 groups; Unstimulated, but not stimulated, saliva flow rates were significantly lower in women than in men	No	There were no statistically significant differences in the oral health parameters of the subjects with NIDDM or NIDDM+CVD compared with age- and sex-matched healthy controls	Although a significant negative correlation was found between the number of medications used and unstimulated saliva flow rate, no relationship was found with caries experience; No correlation was found between medication use and stimulated saliva flow rate
Närhi et al.	1999	Subjects generally healthy, but presented with a range of medication use	110 subjects, mean age 83 ± 5 y at 5-year follow-up, 77F, 33 M	Finland; Mean number of medications used daily was 2.3 ± 1.7	During the 5-year follow-up the number of teeth decreased, leading to a significant increase in DMFT but not decayed root surfaces (DRS); Root caries incidence (RCI) was significantly increased during follow-up; Between baseline and follow-up, stimulated whole saliva flow rate was significantly lower (1.44± 0.84 vs. 1.26± 0.78 ml/min, respectively); Buffer capacity was significantly higher at follow-up ($p<0.05$); Based on logistic and multiple regression analysis, stimulated whole saliva flow rate and buffer capacity were not significant predictors of DMFT, RCI or tooth loss	No	None of the salivary factors correlated with the root caries incidence or the number of teeth lost during the five-year follow-up	Observed changes in salivary flow rate and buffer capacity were not clinically relevant given that values can be considered to be within normal limits
Näsman et al.	1994	Various childhood malignancies and immuno-deficiency; Gaucher's disease; Bone-marrow transplant (BMT)	Bone marrow transplant (BMT) group, 19 subjects, mean age 11.9 ± 3.9 y, 11F, 8M; Chemotherapy (CY) group, 57 subjects, mean age 11.7 ± 4.7 y, 24F, 33M; Control group, 19 healthy age- and sex-matched subjects, mean age 11.9 ± 3.9 y, 11F, 8M	Sweden; Article focus is on different forms of anti-neoplastic therapy; BMT group received concomitant total body irradiation (TBI); CY group	No differences were observed in DFS, DS, CI, dfs, ds or ci for any of the three groups; Salivary buffering capacity for both BMT and CY subjects was significantly lower than in controls; BMT subjects also had significantly lower flow rates (0.7± 0.4 ml/min) than the CY (1.1± 0.5 ml/min) or control groups (1.3± 0.6 ml/min)	No	Despite the diminished flow rate and buffering capacity, no increased caries prevalence was observed in children subjected to anti-neoplastic treatment	The varying fluoride/ chlorhexidine regimens among the groups may have confounded the results; the BMT group appeared to receive a more intensive fluoride/chlorhexidine regimen

				received no radiation to teeth or jaws; Both groups had ≥3 y survival post-treatment				
Naspitz et al.	1999	Subjects generally healthy	49 healthy 3-5-year-old children exhibiting deciduous dentition were divided into 3 groups: children without caries (dmfs=0, n=20), children with 1 or 2 surfaces with carious lesions (dmfs 1-2, n=15), children with rampant caries (dmfs 12-46, n=14)	Brazil; Saliva samples from 4 healthy adults were used as controls in the assays	Total secretory IgA and the anti-S. Mutans IgA, IgM, and IgG antibody levels were not significantly different among the 3 groups; Lower numbers of S. mutans were found in the no-caries group in relation to the low- and high-caries groups; Immunologic profiles were different between the children and adults	No	The saliva of children may exhibit a specific immunologic immaturity	Data from this study do not support a relationship between the secretory immune system and dental caries
O'Sullivan and Curzon	2000	Subjects generally healthy	Study group consisted of 103 children with erosion, age range 3-16 y; Control group consisted of age- and sex- matched non-erosion individuals who were subdivided into caries-free (no clinical caries or conventional restorations) and caries-active (clinical caries or ≥2 restored surfaces) subgroups	United Kingdom	No statistically significant differences were found in unstimulated and stimulated salivary flow rates among the 3 groups; Significantly fewer caries-active children (19%) had high buffering capacity (final pH>6.5) than caries free-children (51%); Caries-active children had lower pH values for both unstimulated and stimulated saliva, but these were not significant; Risk for erosion in a caries-active individual was less than in one that was caries-free	Yes	Individuals with erosion have a caries risk similar to caries-free individuals	Data support a role for salivary buffer capacity in decreasing caries risk because caries-active children generally had lower buffer capacity than caries-free children
Öhrn et al.	1999	Anorexia nervosa; Bulimia nervosa; Medication use	81 patients, 79 F, 2 M, age range 17-47 y, mean age, 25 y; 52 healthy controls, 48 F, 4 M, age range 19-41 y, mean age 24 y	Sweden; Eating disorders were diagnosed based on American Psychiatric Association's DSM III-R criteria	Significant differences were found between patients with eating disorders and healthy subjects for: unstimulated salivary flow rate ($p<0.001$); stimulated saliva buffer capacity ($p<0.05$); and DMFS and DFS indices ($p<0.01$); Eating disorder patients also had significantly higher salivary mutans streptococci and lactobacillus counts; Erosive tooth wear was significantly related to the number of years of binge eating	Yes	Compared to age-matched individuals, subjects with diagnosed eating disorders are more susceptible to both dental caries and erosion	Dietary preferences and antipsychotic medication use among some eating disorder subjects may have influenced the reported results

Pajari	1988	Various childhood malignancies	37 children status post cancer chemotherapy, mean age 11.6 y, age range 5-20 y, 18 children with ongoing cancer therapy, mean age 6.3 y, age range 2-14 y; Age-matched healthy controls	Finland; with one exception, no child received radiation to the jaws	Caries incidence was high during the malignant disease but fell to control levels after successful remission; Xerostomia and salivary flow rate alterations were transient; Only slight differences in salivary immunoglobulin levels were observed; Children with cancer had more lysozyme than controls; Salivary pH values were significantly lower in the children with cancer and in those cured of cancer	Possibly	The findings suggest that children with cancer are more at risk for caries , in terms of prevalence and incidence	Author acknowledges that it remains to be established if the state of malignancy or its treatment is the more critical factor
Pandey et al.	1990	Subjects generally healthy	Group I, 35 children with non-rampant caries (mean DMFS/dfs=4.57); Group II, 35 children with rampant caries (mean DMFS/dfs=11.25); Group III, 35 children without caries (mean DMFS/dfs=0); age range of all three groups 5-15 y, both sexes were included	India	Mean salivary phosphorous concentration and alkaline phosphatase activity was higher in patients with rampant caries (group II) than in the those with non-rampant caries (group I) and with no caries (group III); Mean salivary phosphorus content in group III was 13.08± 3.42mg% as compared to group II (28.11 ± 24.51mg%, $p<0.001$) and group I (14.04 ± 3.58mg%, $p<0.01$); Alkaline phosphatase activity for group II was significantly higher (4.308 ± 5.73 activity units (AU), $p<0.01$) than in group III (1.958 ± 1.53AU) and in group I (3.945 ± 5.63AU, $p<0.01$)	Possibly	Higher phosphorus concentration and alkaline phosphatase activity were found in patients with rampant caries as compared to that with non-rampant and control groups	Standard deviations were quite large; Several inconsistencies in the data presentation make interpretation difficult
Parkash et al.	1994	Subjects generally healthy	126 caries-positive subjects, 58 F, 68 M; 55 caries-negative subjects, 25F, 30M; Both groups mean age 12.5 y, age range 10-15 y	India	Compared with control subjects, children with caries had lower salivary levels of total IgG (160 ± 0.7 vs. 340 ± 2.9 mg/dl) and total IgA (130 ± 0.5 vs. 410 ± 3 mg/dl); Significantly more children with caries (75%) than without caries (22%) had high levels of salivary anti-S. mutans IgA; Total and specific salivary IgM were not different between the caries and no-caries groups; Compared with control subjects, children with caries had higher serum levels of IgG (1350 ± 9.9 vs. 1110 ± 6.7 mg/dl) and IgA (260 ± 1.8 vs. 190 ± 1 mg/dl)	Yes	Humoral immune response may play a major role in caries risk	Definition of caries and no-caries status of subjects was not defined; Salivary specific IgA appeared to be proportionally associated with caries prevalence
Pedersen et al.	1999	Primary Sjögren's syndrome (pSS)	16 pSS patients, 14F, 2M, age range 40-82 y; 27 healthy controls, subdivided into 13 young healthy individuals (12F, 1M, age range 20-33 y) and 14 aged controls (13F, 1M, age range 39-70).	Norway; All patients met the European classification criteria for pSS; Patients were equally distributed according to having or not having salivary lymphocytic infiltrates (i.e., focal score, FS) and/or	pSS patients with lymphocytic infiltrates in salivary glands (FS) and/or the presence of certain autoantibodies (AB) generally had lower salivary secretory rates than patients without FS and/or AB (P=0.01 for unstimulated whole saliva and stimulated parotid saliva) and age-matched healthy controls (P=0.001); pSS patients with FS and/or AB had higher DMFT/DMFS than patients without FS and/or AB and healthy controls ($P<0.01$); There were no significant differences in the content of Na, K, statherin and aPRPs between the groups.	Yes	pSS patients with FS and/or AB had lower salivary secretion rates and higher DMFT/DMFS than healthy controls and pSS patients without FS and/or AB	The presence of lymphocytic infiltrates in salivary glands and/or the presence of certain autoantibodies in pSS patients may affect saliva characteristic and caries scores

				specific autoantibodies (AB)				
Pienihäkkinen	1987	Subjects generally healthy	284 children, age range 7-12 y, categorized < 9y and >10y; Patients were part of another study: 139 from xylitol group and 145 from a combined fluoride and control group	Hungary	Buffering capacity contributed significantly to caries incidence prediction in the combined fluoride and control group (odds ratio 2.5, 95%CI 1.2-5.2), but did not contribute at all to caries incidence prediction in the xylitol group; Presence of incipient caries and the level of salivary lactobacilli and yeasts were generally stronger predictors for both groups	Possibly	Combination of incipient caries lesions and salivary lactobacilli and yeast has good ability to distinguish subjects with high and low caries increment	Age and gender effects on salivary buffering capacity appear to lower its value as an indicator of high caries increment
Pienihäkkinen et al.	1987	Subjects generally healthy	350 subjects, age range 7-12 y, categorized < 9y and >10y; Patients were part of another study: 135 from xylitol group and 215 from a combined fluoride and control group	Hungary	The sole use of buffering capacity was determined to be a weak caries test in children; Similar buffering values were observed in 71% of all subjects, girls generally had a lower buffering capacity than boys; Flow rate and buffering capacity were significantly correlated with each other	No	As a caries screening test buffering capacity was not a good way of distinguishing subjects with high and low caries increments	The study group and experimental design appears to be the same as in Pienihäkkinen et al., 1987, but the results relative to buffer capacity appear to be different
Pohjamo et al.	1988	Diabetes (IDDM and NIDDM)	50 adult diabetics were divided into 3 groups: 10 well controlled, 24 moderately well controlled, 9 poorly controlled (data on diabetic control not available for 7 subjects); 52 age- and sex-matched healthy controls; Age distribution of all subjects was: 38 age <30 y, 35 age 30-40 y and 29 age >40 y.	Finland; Mean duration of diabetes was 9.0±1.0 years; Distribution of subjects by medication (insulin, oral drugs, diet) was similar in all 3 diabetes subgroups	Mean saliva flow rate and buffer capacity did not significantly differ between the diabetes and control groups; There was no statistically significant difference in caries experience between the diabetes group as a whole and the controls, however, poorly controlled diabetics tended to have a higher caries prevalence than the well-controlled ones	No	The level of control of diabetes may contribute to caries development	Saliva flow rates and buffer capacity appeared normally distributed in both the diabetes and control groups

Raitio et al.	1996 a	Subjects generally healthy	181 subjects total; 80 F, 101 M, mean age at initial examination 13.3y, age range 11.9-14.9y	Finland	Salivary flow rate and buffer capacity had no significant predictive value in the multifactorial model; Gender differences were observed for the various predictive factors	No	Past caries experience, white spot lesions, presence of Candida, salivary sucrase activity and age appear to be good predictors of caries risk	Pre-existing caries appeared to be one of the best predictors of caries incidence; Only approx. 20% of subjects developed new carious lesions
Raitio et al.	1996 b	Subjects generally healthy	181 subjects total; 80 F, 101 M, mean age 13.3y, age range 11.0-14.9y	Finland	Salivary secretion rate and buffer capacity had no association with ΔDFS; 21% of the subjects developed new caries; Of the variables evaluated, past caries experience (p=0.002), white-spot lesions (p=0.01), lactobacilli counts (p=0.02), Candida counts (p=0.006), and salivary sucrase activity (p=0.02) were significantly associated with ΔDFS; In contrast, visible plaque, gingivitis and S. mutans counts had no association with ΔDFS	No	Data indicate the importance of past caries experience and white spot lesions in caries prediction	The lack of association of salivary flow rate, buffer capacity, plaque index or gingival index with caries increment is consistent with previous studies; Gender differences were observed for salivary secretion rate and buffer effect
Ravald and List	1998	Primary Sjögren's syndrome (pSS)	21 pSS patients, 20F, 1M, mean age 64 y, age range 44-75 y; 21 controls, 20F, 1M, mean age 65 y, age range 44-78 y	Sweden	pSS patients had significantly more DF crown surfaces (63±25.8 vs. 43±21.3) and more inactive root caries (4.4±5.4 vs. 0.5±0.9) than did the control patients; Mean unstimulated salivary secretion rate was 0.09±0.16 ml/15 min in the pSS group and 3.33±2.81 ml/15 min in the control group; Mean stimulated secretion rate was 0.16±0.15 ml/min and 1.47±0.64 ml/min, respectively	Yes	pSS patients face a high risk of developing both coronal and root caries due to xerostomia	In this study the observed differences in caries between pSS and control groups was unrelated to salivary microbial counts since only minor differences were found between the two groups
Ravald et al.	1993	Subjects generally healthy	Initially 195 treated periodontal disease patients were evaluated (i.e., at baseline examination 12 y earlier), subjects were gradually lost over time; In the present study 27 subjects were evaluated at multiple time points over 12 years; 13 F, 14 M, mean age 59.2 ± 8.2 y, age range 47-79 y	Sweden	No significant differences were found in flow rate, buffer capacity or oral sugar clearance time between subjects with low (≤ 5) or high (>5) incidence of caries 12 years after periodontal treatment	No	Risk of root caries in maintained periodontally-treated patients as a group is a minor problem, however, some individuals may have a high incidence	The annualized incidence of caries was rather low in general

Riviere and Papagiannoulis	1987	Subjects generally healthy	Children age 6-13 y, 29 caries-prone (CP) subjects, mean age 8.5 ± 1.8 y, 17F, 12M; 34 caries-free (CF) subjects, mean age 9.2 ± 2.0 y, 21F, 13M	United States; Subjects defined as: Caries-prone (CP), DFS ≥1; Caries-free (CF), DFS=0	CP and CF children had no significant differences in the levels of salivary IgA, IgG and IgM, regardless of the presence or absence of indigenous S. mutans; Except for a minor difference in IgG binding specificities within the CP group, the CP and CF children had no significant differences in the binding activities of salivary IgA, IgG and IgM to seven serotypes of S. mutans, including the indigenous type	No	The data do not support the caries-protective role of a humoral immune mechanism that involves the binding of salivary immunoglobulins to S. mutans	The caries risk definitions used in this study may not adequately distinguish between low and high risk individuals; The high degree of cross-reactivity of salivary antibodies with other types of oral bacteria may mask critical antigen-antibody reactions that may be present
Rose et al.	1993	ND/NA	40 subjects total, age range 7-11 y; 20 caries-susceptible (CS) children; 20 caries-resistant (CR) children	United States; Caries risk defined as: Caries-resistant (CR) DMFS ≤1 and Caries-susceptible (CS) DMFS > 5	Whole saliva from CR children had significantly higher levels of IgA antibodies to S. mutans than saliva from CS children; Salivary S. mutans numbers were significantly higher in the CS group (31.2% of total strep.) than in the CR group.(1.6% of total strep.)	Yes	IgA antibody to S. mutans may play a role in natural protection from dental caries in children	These data for children are in agreement with similar studies of adults
Rose et al.	1994	Subjects generally healthy	Children aged 7-11 y; 20 caries susceptible (CS), mean age 9.46 ± 1.34 y, 8F, 12M; 21 caries resistant (CR), mean age 9.78 ± 1.41 y, 3F, 18M	United States; Subjects were defined as: Caries-resistant (CR) DMFS ≤1 and Caries-susceptible (CS) DMFS > 5	CR children had significantly greater ($p \leq 0.05$) anti-S. mutans specific IgA levels in whole saliva than did the CS children; No significant differences were found in anti-S. mutans specific IgA levels in parotid saliva from CR and CS children; No significant differences were found in total IgA levels in either whole saliva or parotid saliva from CR and CS children; Whole saliva from CS had significantly more S. mutans (31.2% of all mutans) than whole saliva from CR (1.6% of all mutans); Whole saliva from CS had significantly less IgA to S. mutans than whole saliva from CR ($p \leq 0.05$)	Yes	Anti-S. mutans IgA antibodies may protect children from caries; the source of these antibodies may be the sublingual, submandibular or minor salivary glands	Data support the belief that the specific type of salivary antibody is more clinically significant than the total levels of antibody; Data are same as previous abstract (Rose et al., 1993)
Ruhl et al.	2000	ND/NA	30 children with early childhood caries (ECC), which is a rampant form of dental caries; 21 control children without caries	Germany	The resulting electrophoretic patterns (dendrograms) of protein and glycoprotein bands from the various donors were compared with each other in a database; The dendrograms obtained showed no clear separation of the study groups	No	At least with the methods used in this study, no significant correlation between an individual's risk for dental caries and the composition of salivary	A certain clustering of patients with ECC and caries-free controls could be observed

							proteins and glycoproteins could be found	
Ryberg et al.	1987	Asthma; Medication use	24 asthmatic children, 13 F 11 M; age range 10-20 y; control subjects were age-and sex-matched friends of the asthmatic subjects (n=24)	Sweden	No statistical difference in DFS between both groups; whole saliva flow rate in controls was 1.77 $\pm$ 0.91 vs. 1.31 $\pm$0.55 ml/min in asthmatics ($p<0.05$); Parotid saliva flow rate in controls was 0.67 $\pm$ 0.43 vs. 0.43 $\pm$ 0.42 ml/min in asthmatics ($p<0.05$); no differences in pH and buffer capacity were seen; total protein and amylase in stimulated parotid saliva of asthmatics was significantly lower than in controls	No	Asthmatic children had higher DFS, but these were not significantly different from healthy controls	2 asthmatic children and 6 controls had no carious lesions
Ryberg et al.	1991	Asthma; Medication use	21 asthmatic children, 12F, 9M, mean age 19.6 $\pm$ 2.4 y, age range 14-24 y; Control subjects were age-and sex-matched friends of the asthmatic subjects	Sweden	In the asthmatic group the secretory rates of stimulated whole and parotid saliva decreased 20% and 35%, respectively, compared to the controls; Asthmatic patients had decreased output per min. of total protein and various individual salivary components; ΔDFS was significantly increased in the asthma group	Possibly	Asthmatic patients treated with β_2-adrenoceptor agonists have an increased caries susceptibility due to an impaired saliva secretion caused by the use of β-adrenergic agonists	The present study represents the 4-year follow-up to the earlier study of Ryberg et al. (1987); Mean whole saliva flow rates in both low -caries and high-caries subgroups of asthmatics were within normal limits and not significantly different
Rytömaa et al.	1998	Bulimia nervosa	35 Female bulimics, mean age 25.3 $\pm$ 6.8 y; 105 Female controls matched for age, sex and education, mean age 25.7 $\pm$ 7.0 y	Finland	There were no significant differences between bulimic subjects and healthy controls for DMFS and DS; A significant difference was found between bulimic subjects and healthy controls for pre-cavitated lesions (DSini, $p<0.01$); There were no significant differences between bulimic subjects and healthy controls for unstimulated whole saliva flow rate, stimulated whole saliva flow rate and salivary buffer capacity; However, the number of subjects with low unstimulated salivary flow rate (< 0.2 ml/min) was 3-4 times higher among bulimics than controls ($p<0.05$); Bulimic subjects also had more self-reported dry mouth symptoms than controls ($p<0.001$)	Possibly	Severe dental erosion and dental caries were significantly commoner among bulimics than controls	The relationship between pre-cavitated lesions and a tendency for lower salivary flow rate in bulimics is unclear from these data

Seemann and Kage	1997	Subjects generally healthy	63 total subjects, age 10-year-old; 28 subjects in the no caries group, Grp(-); 35 subjects in the high caries prevalence group, Grp(+)	Germany; Caries risk defined as: Caries-positive (DMFT≥4) and Caries-negative (DMFT+dmft= 0)	Grp(+) had significantly ($p<0.05$) higher concentrations of anti-S. mutans IgA compared to Grp(-); For eight different lectins, only binding of peanut agglutinin (binding specificity: β-D-galactosyl-residues) to a complementary glycoprotein was significantly ($p<0.05$) more inhibited by saliva of Grp(-) children compared to saliva from Grp(+) children	Possible	Caries risk could be inversely related to the concentrations of salivary glycoconjugates with terminal galactosyl residues	Data support a protective role of specific IgA antibodies; Also, since S. mutans can adhere to the teeth via an adhesin with galactosyl specificity, the higher presence of these in caries-negative children might be protective against caries
Sepet et al.	1998	Acute Lympoblastic Leukemia (ALL)	41 ALL patients, 13F, 28M, age range 4-16 y, divided into 3 subgroups according to length of maintenance period: <12 months, 18 subjects, mean age 8.2±2.9 y, age range 4-14 y, 4F, 4M; 12-24 months, 11 subjects, mean age 7.4±2.1y, age range 5-11 y, 7F, 4M; >24 months, 12 subjects, mean age 10.9±2.5, age range 7-16, 3F, 9M; 20 control subjects, mean age 9.0±2.5 y, age range 4-13 y, 10F, 10 M	Turkey	There was no significant difference in dental caries experience and salivary flow rate between leukemia and control groups; pH scores of all groups were within normal limits despite the finding of a statistically significant difference between the children who were in maintenance therapy for 12-24 months and less than 12 months and also the control group	No	There is no indication that oral hygiene measures should be discontinued during the treatment of ALL patients	The length of remission from ALL does not appear to influence caries prevalence or result in clinically relevant changes in salivary flow or pH; Children with leukemia received chemotherapy but not radiation therapy
Sgan-Cohen et al.	1992	Subjects generally healthy	Two groups of children: 68 age 5-6 y, 31 F, 37 M and 32 age 12 y, 13 F, 19 M; 70 adults 35-45 y, 29 F, 41 M; 20 controls, 35 –45 y, 6 F, 14 M	Ethiopia and Israel; Control subjects were only for comparison of saliva and bacterial variables	5-6 y children, 86.8% caries-free (79%-95% at the 95% confidence interval (CI)); 12 y children, 81.8% caries-free (63%-93% at the 95% CI); Adults, 54% caries-free (34%-58% at 95% CI); Mean DMFT was significantly lower in 12 y children (0.31) than adults (1.27); No significant differences in total counts of salivary bacteria between study subjects and control, but the number of Lactobacilli was significantly higher in the study group than in control ($p< 0.001$); Initial pH values were not significantly different between study subjects and controls, however, the drop of pH after applying 2% sucrose was significantly higher in the study group within 30 min, but not after 60 min; Flow rate was higher in the study group (1.93 ml/min) than controls (1.16 ml/min)	No	Low level of caries in the study group can be attributed to an almost sugar-free diet and high salivary flow, but not to composition of oral microflora	Salivary flow rate in both groups was within normal limits; No DMFT data on the control subjects were presented; Data presented for the study group were pooled from male and female subjects who showed significant sex-oriented difference with respect to flow rate and caries prevalence

Shapira et al.	1991	Down syndrome (DS); Non-Down Mental Retardation (MR) [adult subjects]	3 study groups evaluated; 12 patients with DS, age range 20-48 y; 12 patients with MR, age range 21-37 y; 11 healthy controls, age range 20-49 y; the groups were similar in gender	Israel; no subjects had chronic physical diseases	The pH levels did not differ significantly among the 3 groups (range 6.6-6.8 in all 3 groups); mean DMFS was significantly lower in DS (15.9) than in MR (29.7) or healthy subjects (33.7)	No	The lowest DMFS score was observed in the Down's syndrome group	Teeth with periodontal diseases were extracted, possibly confounding results because Down's subjects had higher periodontal disease score
Siamopoulou et al.	1989	Juvenile chronic arthritis (JCA)	16 JCA patients, 7F, 9M, mean age 9.3 y, age range 6-14 y; 83 healthy control children matched for age, sex and socioeconomic status	Greece; Mean duration of JCA 4.6 y; 3 JCA subjects had disease of systemic onset, 9 polyarticular, and 4 pauciarticular	Mean DMF Index in JCA children was almost twice as high as that in the control group (6.0 vs. 3.2, respectively); Parotid flow rates as well as urea and chloride levels were not significantly different between the 2 groups; Concentrations of calcium, phosphate, potassium, lysozyme and total IgA were significantly decreased in the JCA group compared with controls (all $p<0.05$); Concentrations of sodium and amylase were significantly higher in the JCA group (all $p<0.05$)	Possibly	These data could provide an explanation for the increased caries seen in JCA	Authors' acknowledge that the data are preliminary in explaining how biochemical abnormalities in saliva may increase caries risk in children with JCA
Siamopoulou-Mavridou et al.	1992	Thalassemia major (TM)	21 TM patients, 9F, 12M, mean age 11.9±3.7 y; 83 healthy controls, matched for age, sex and socio-economic status, not receiving any medication	Greece; the mean duration of TM disease was 7.9 y (5-13 y)	Dental caries experience was significantly higher ($p<0.001$) in the TM group (Median DMFT=7.0, 95%CI 4.0-9.5) compared with healthy controls (Median DMFT=2.9, 95%CI 1.3-4.7); Parotid saliva flow rates in TM patients were not significantly different from those in the healthy controls; Median saliva concentrations of urea, inorganic phosphorus and IgA were significantly lower in the TM patients than in the controls; Median sodium concentration was higher in the TM group; Median concentration of lysozyme was lower in the TM group, but the difference was not statistically significant.	Possibly	Differences in concentrations of biochemical components in parotid saliva of TM patients may contribute to the significantly increased prevalence of caries	The lower level of IgA in the parotid saliva of TM patients may allow increased microbial proliferation that could be involved in the increased dental caries experience of TM patients.
Soderholm and Birkhed	1988	Subjects generally healthy	68 patients total; 38 caries-active subjects who developed 1-9 new proximal caries lesions and received 6-21 new fillings during the previous 4 y, mean age 56.1 y, age range 39-74 y; 30 caries-inactive subjects who had not developed new lesions and had not received more than 3 new fillings during the previous 4 y, mean age 55.5 y, age range 40-74 y	Sweden; Examination was done once per year with total of 3 examinations during the 2-year period	There was no significant difference in salivary flow rate or buffer capacity between the 2 groups; Of the other variables studied only DMFS ($p<0.001$), dietary score ($p<0.05$) and number of S. mutans in saliva ($p<0.05$) differed significantly between the two groups; Number of S. mutans showed the highest sensitivity value followed by dietary score	No	Despite group differences between caries activity and some unfavorable predictor values it would have been difficult to predict the caries-active patients on an individual basis	The median values of all studied variables tended to be more favorable in the caries-inactive than in the caries-active group, but variations precluded clear prediction of risk activity in individual subjects

Soto-Rojas et al.	1998	Primary Sjögren's syndrome (pSS) and Secondary Sjögren's syndrome (sSS)	21 subjects with pSS, 20 F, 1 M, mean age 56.9 ± 11 y; 29 subjects with sSS, 28 F, 1 M, mean age 47.4 ± 13 y; 31 controls for pSS and sSS, 29 F, 2 M, mean age 49.8 ± 10 y	Mexico; Age difference between pSS and sSS was significant (p=0.03)	Self-reported oral dryness was significantly lower in both pSS and sSS groups compared to controls; occlusal decay and cervical decay were significantly higher in both pSS and sSS compared to controls	Yes	Significant differences were found between SS and healthy subjects	Cervical or atypical caries was found in 83% SS patients
Stabholz et al.	1991	Down syndrome (DS); Non-Down Mental Retardation (MR) [preadolescent subjects]	3 groups evaluated; 32 children with DS, age range 8-13 y; 19 patients with MR, age range 8-13 y; 30 healthy controls, age range 8-13 y; the groups were similar in gender	Israel	The pH levels of the DS and MR groups were significantly lower than the healthy controls, but not significantly different from each other (DS 6.7 ± 0.6, MR 6.8 ± 0.6, control 7.1 ± 0.4); mean DMFS was significantly lower in DS (1.2 ± 4.0) than in both MR (15.6 ± 19.2) and healthy subjects (14.5 ± 8.3)	No	No relationship between caries indices and pH values was found among all 3 groups	Unclear why DS and MR groups had significantly different DMFS but not pH; clinical significance of pH data unclear; 84% DS children were caries free
Stiefel et al.	1990	Chronic mental illness (CMI); Medication use	37 CMI subjects, 13 F 24 M, mean age 33.4 ± 8.6 y; 29 control subjects, 10 F 19 M, mean age 30.0 ± 8.6 y	United States; All CMI subjects received psychotropic medications (mean 3.8 drugs over 10.3 years)	CMI group had significantly higher self-reported dry mouth, coronal smooth surface caries and lower salivary flow ($p<0.05$); no significant differences evident in M and F components of DMFS; 70.3% CMI recorded dry mouth; no significant differences were seen in salivary flow or caries in patients either taking or not taking lithium	Yes	Significant increase in risk factors in community dwelling CMI compared with a control group that showed dental neglect	Difficult to follow exact number of saliva samples and subjects evaluated; Salivary collection method questionable in that weight and volume over time was not presented
Stiefel et al.	1993	Spinal cord injury (SCI)	17 SCI patients, 2 F 15 M, mean age 32.3 ± 4.9y, age range 26-40y; 17 healthy control, 6 F 11 M, mean age 31.1 ± 6.2y	United States; SCI subjects were 8-14 years post injury (16 quadriplegic, 1 paraplegic)	No significant inter-group differences were seen with respect to salivary flow and DMFS	No	No significant differences between spinal cord injury and control subjects were noted	Unclear whether saliva flow rate is reported as ml/min or ml/5 min
Sullivan	1990	Subjects generally healthy	87 children examined at 5, 6, and 7 years of age between 1984 and 1987	Sweden	The correlation between caries incidence and salivary flow rate and buffer capacity was found to be very low; Mean salivary secretion rates at ages 6y and 7y were 0.8 and 0.9 ml/min, the logarithmic mean values of buffer capacity at ages 5y, 6y, and 7y were 4.7, 5.1, and 5.0, respectively	No	Secretion rate and buffer capacity of stimulated whole saliva have too weak a relationship with caries incidence in healthy children to be of any real value as caries predictors	Caries incidence between ages 5 and 7 (Mean 3.3) may be too low to discern any effect due to salivary parameters

Sullivan and Schröder	1989	Subjects generally healthy	89 children examined at 5, 6, and 7 years of age	Sweden	Buffer capacity was a poor predictor of caries incidence (sensitivity=35, specificity=55); Saliva secretion rate could not be measured at 5 years of age; Of the variables evaluated, the S. mutans count had the best combination of sensitivity and specificity, while the values for lactobacilli and buffer capacity varied	No	Changes in dietary and oral hygiene habits as well as in the level of restorative treatment may have confounded the results	Presumably the study subjects and experimental design are the same as in Sullivan, 1990, which provided data on salivary flow rates measured between ages 6 and 7 years
Sundh et al.	1993	Crohn's disease; Medication use	Three groups were identified; 13 with ongoing symptoms of Crohn's Disease (acute); 12 asymptomatic Crohn's patients (not acute); 12 medically healthy controls age- and sex-matched to the non-acute group	Sweden; Acute group had no or only minor surgical loss of small intestine; non-acute group had greater than 50% surgical loss of small intestine	No differences were found among the groups regarding salivary flow rate, total protein, or antimicrobial proteins; DS value was higher in the non-acute group than the control ($p< 0.01$)	No	Crohn's disease patients had an increased caries risk that is not associated with saliva	68% of Crohn's patients (acute and non-acute) used some kind of drug vs. 0% of controls
Sundin et al.	1992	ND/NA	75 total 15-year-old subjects examined at baseline; 69 of these re-examined 3 years later at age 18 y	Sweden; Three groups were identified at baseline: No-caries (DFS=0, n=30); Moderate caries (DFS 4-6, n=25); and High caries (DFS 12-15, n=20)	Salivary flow rate and oral sugar clearance time were poorly correlated with 3-year caries incidence; Simple linear correlations between caries incidence and the different variables showed that lactobacilli count ranked first, sweets second and mutans streptococci count third. The r value for caries incidence and the consumption of sweets increased in subgroups with combinations of poor oral hygiene, a high intake of other sugary products and a low salivary flow rate	Possibly	Consumption of sweets is still one of the most important caries related factors	Based on this study it appears that dietary and salivary microbial factors outweigh salivary flow rate and sugar clearance rate effects, especially when the latter are considered to be within normal limits
Swanljung et al.	1992	Insulin dependent diabetes mellitus (IDDM)	85 IDDM patients; 46 F, 39 M; mean age 15.1 $\pm$ 1.5y; age range 12-18y; 85 age- and sex-matched medically healthy controls; mean age 15.1 $\pm$1.6y	Finland; well-controlled diabetics; mean duration of diabetes 5.2 $\pm$ 3.5 y	No significant differences in caries indices or saliva values between diabetic adolescent subjects and their controls; for both caries indices and saliva values, there were no significant effects due to duration of IDDM, gender, age, oral hygiene habits or fluoride use	No	No differences in salivary or caries data exist between well controlled IDDM patients and healthy controls	Diabetic controls is questionable because mean glycosylated hemoglobin value (10.9%) appears high; standard deviation for caries indices and saliva values appear high

Tenovuo et al.	1986	Insulin dependent diabetes mellitus (IDDM)	35 dentate diabetics; 11 F, 24 M; mean age 30.4 y, age range 17-61 y (12 smokers); 35 age- and sex- match medically healthy controls (14 smokers)	Finland; mean duration of diabetes 14.0 ± 9.1 y; median age at diabetes onset 14 y (range 3-42 y); in a separate substudy a correlation between salivary and serum glucose levels was examined in 7 hospitalized IDDM patients, aged 23-43 y (4 F, 3 M; 110 total saliva-blood samples)	When controlled for age, diabetics ≥31 y had significantly higher DS than healthy controls (13 vs. 3, respectively; p< 0.01); when controlled for last comprehensive dental visit, diabetics had less mean FS (25.4 ±16.5) than healthy controls (34.0 ± 15.2) (p<0.05); salivary values did not differ significantly between the two groups; large individual variations in salivary glucose levels were observed; salivary values showed no correlation with subject age, diabetes duration or age of onset	No	In spite of their noncariogenic dietary habits, diabetic adults have the same risk of caries as non-diabetic subjects	No quantitative measure of diabetic control; wide variation in salivary glucose levels
Touyz et al.	1993	Anorexia nervosa; Bulimia nervosa	45 female subjects divided into 3 groups; 15 anorexia patients, mean age 20.1± 8.3 y; 15 bulimia patients, 19.1 ± 3.8 y; 15 controls, mean age 22.1 ± 3.3 y	Australia	All three groups had no significant differences in DMFT and salivary flow rates; anorexic and bulimic patients had slightly more acidic saliva (pH 7.1) than did control subjects (pH 7.6) (p<0.001)	No	Patients with anorexia or bulimia have caries risk no different than healthy women of similar age	All patients in the study had been exposed to a fluoridated water supply
Tukia-Kulmala and Tenovuo	1993	Subjects generally healthy	128 school children, 60 F, 68 M, all 11 years old at initial examination	Finland	Intra- and interindividual variations in salivary flow rate were relatively large; buffer effect was significantly lower in girls than boys; the 1-year caries increment correlated inversely with baseline values for flow rate and buffer effect (p<0.001; data not shown)	Possibly	Simultaneous changes in behavioral, hormonal and dietary factors among teenagers make single-point measurements of salivary factors too unreliable for caries-predictive purposes	Caries incidence in the study group was relatively low; Measurements of salivary flow rate and buffer effect are highly variable in subjects of this age

Twetman et al.	1989	Insulin dependent diabetes mellitus (IDDM)	94 IDDM patients, 42F, 52M, mean age 14.0 y, age range 4-19 y; 94 age-, sex- and geographically-matched control children with no systemic disease and no current medication	Sweden	There were no differences in caries experience or buffer capacity between the groups; Flow rate of stimulated whole saliva was significantly ($p<0.05$) lower among the diabetic children (1.2±0.7 ml/min) compared to their healthy controls (1.5±0.5 ml/min)	No	Decreased saliva secretion rate may predispose diabetics to growth of cariogenic bacteria	The stimulated whole saliva flow rates in both the diabetic and control groups were within normal limits
VanWuyckhuyse et al.	1995	Subjects generally healthy	19 caries-susceptible (CS-A) adults, 10F, 9M, median age 65 y, age range 50-74 y; 20 caries-free (CF-A) adults, 9F, 11M, median age 58.5 y, age range 50-83 y; 17 caries-susceptible children (CS-C), 10F, 7M, median age 12 y, age range 10-16 y	United States; Adult patients grew up prior to water fluoridation; Children were caries susceptible and had been exposed to fluoride; Median DMFS (range) was CS-A=48 (23-125), CF-A=0 and CS-C=16 (10-34)	Comparison of CS-A vs. CF-A provided information about the association between caries status and amino acid concentration, unconfounded with age: CF-A group had significantly higher levels of arginine, lysine, histidine and glutamic acid ($p<0.05$), at $p<0.0025$, only the levels of arginine and lysine remained significant; Comparison of CS-A vs. CS-C provided information on the confounding effect of age: CS-A group had significantly higher levels of arginine, proline and tryptophan, at $p<0.0025$, only the level of tryptophan remained significant; Regression analysis of amino acid levels and age with DMFS in CS-A and CS-C groups indicated statistical significance for lysine (CS-A $p=0.035$; CS-C $p=0.044$) but not for arginine (CS-A $p=0.13$; CS-C $p=0.09$)	Possibly	Basic amino acids help neutralize plaque acids and may partially account for higher resting plaque pH in caries-free individuals	Information within the Abstract concerning lysine is not consistent with data presented within the article
Vehkalahti et al.	1996	ND/NA	66 patients, 35F, 31M, mean age 15.2 ± 0.9 y, age range 13.7-16.7 y	Finland; Subjects were deemed caries-susceptible; baseline DMFT=5.7	ΔDFS was correlated with buffering capacity only for boys (-0.34, $p<0.05$); ΔDFS was correlated with stimulated saliva flow rate only for girls (-0.28, $p<0.05$); Collectively, the combination of flow rate and buffering capacity was a moderate indicator of caries incidence; Salivary microbial counts were the strongest indicators for caries increment; Flow rate of unstimulated whole saliva <0.2 ml/min had sensitivity=0.21 and specificity=0.96; Flow rate of stimulated whole saliva <1.0 ml/min had sensitivity=0.26 and specificity=0.93; Buffering capacity final pH <4.5 had sensitivity=0.18 and specificity=0.93	Possibly	The highest sensitivities of salivary tests for caries were found for the presence of high amounts of lactobacilli and mutans species	Relatively few subjects (range 11-23%) had salivary flow rate or buffer capacity deemed to be high risk
Vranić et al.	1991	Subjects generally healthy	43 children with caries, age range 12-15 y; 39 children without caries	Croatia	Saliva from the children with caries had a significantly lower level of arginine (22.02μmol/L) when compared to the children without caries (28.36 μmol/L); Saliva from the children with caries had a complete lack of histidine and its derivatives when compared to controls; Acidic and neutral amino acids predominated in saliva from children with caries whereas basic amino acids predominated in saliva from children without caries	Possibly	A decreased concentration of arginine, and a lack of histidine and its derivatives, might be associated with an increased risk of caries	Data suggest that mineral exchange processes occurring at enamel surfaces may differ in caries-active vs. caries-free individuals; Ranges and standard deviations of amino acid measurements were large

Wiktorsson et al.	1992	Subjects generally healthy	496 subjects total; 260 from optimal fluoride area (group U), 138F, 122M; 236 from low fluoride area (group E), 117F, 119M; age range 30-40 y	Sweden; 53.1% of the optimal fluoride group was deemed caries-inactive; 29.2% of the low fluoride group was deemed caries-inactive	Caries activity was significantly lower among those subjects from the optimal fluoride area; Buffer capacity but not flow rate was significantly lower in the caries-active subjects; No significant differences in buffer capacity or saliva flow rate were seen between groups U and E	Possibly	The single decisive fact ruling caries activity appears to be the fluoride concentration in the drinking water	No data presented on how active vs. arrested caries was determined (reference is made to a previous publication)
Wöltgens et al.	1992 a	Subjects generally healthy	548 children, age range 4-16 y; 252F, mean age 10.5±0.1 y; 296M, mean age10.3±0.1	The Netherlands	Caries progression was negatively related with P concentrations in both unstimulated and stimulated saliva for girls; For boys a negative correlation was found between caries progression and flow of stimulated saliva; Concentrations of Ca, P and Mg in saliva were significantly related to cariogenic events in the enamel surfaces of girls, and to salivary viscosity of boys	Possibly	The results underline the importance of salivary flow in caries progression for boys and P for girls	Reasons for gender differences found in this study are unknown
Wöltgens et al.	1992 b	Subjects generally healthy	373 children, 170F, 203M, mean age 10.4±0.1 y, age range 4-15 y	The Netherlands	It was confirmed radiologically that for girls the P concentration in saliva and for boys the amount of resting saliva are important for preventing extension of caries into deeper layers of enamel; Differences in sensitivity between clinical and radiological techniques used to diagnose cariogenic changes were observed	Possibly	For girls, the P concentration and buffer capacity of saliva are highly correlated with caries susceptibility whereas for boys it is the flow rate and Snyder test	This study reports radiographic findings from the same teeth in the same children as in Wöltgens et al. 1992; Summarizing both clinical and radiographic data it appears that gender differences exist between caries progression and certain salivary parameters
Wood and Lee	1988	Systemic sclerosis/ Scleroderma	31 F patients, mean age 51.9 ± 11.7 y; 30 F controls, mean age 50.3 ± 12.2 y (for intraoral radiographs comparison); 30 F controls, mean age 50.2 ± 12.0 y (for extraoral radiographs comparison w/o oral examinations)	Canada; 15 patients with restricted scleroderma, 16 patients with diffuse scleroderma.	Mean ± SD of DMFS for scleroderma patients (w/ and w/o xerostomia) and controls, respectively: 101 ± 36, 77±36, 77±35; Mean ± SD of number of carious teeth for scleroderma (w/ and w/o xerostomia) and controls, respectively: 4.9 ± 6.1, 0.6 ±1.4, and 1.8±2.6; A negative association between xerostomia and caries prevalence was observed ($p<0.05$)	Yes	Xerostomia was present in 70% of scleroderma patients (vs. 10% in control subjects) and was associated with increased frequency of dental caries.	No patients were taking any anticholinergic drugs

Younger et al.	1998	Subjects generally healthy	Elderly subjects, 45F, 63M, divided into 2 groups: 39 subjects with positive root caries (RC+) experience, mean age 72.4 ± 7.1 y; 69 subjects with negative root caries (RC-) experience, mean age 73.3 ± 7.9 y	United States; Subjects were part of the Baltimore Longitudinal Study of Aging; RC+ and RC- groups had DFS (root)=4.1 ± 2.7 and 0.0, respectively	The 5 salivary flow rates examined were poor predictors of the number of carious root lesions; Flow rates (ml/min) of unstimulated parotid saliva, stimulated parotid saliva, unstimulated sublingual/submandibular saliva, stimulated sublingual/submandibular saliva, and stimulated whole saliva were not significantly higher in the RC- group (0.06 ± 0.08, 0.31 ± 0.27, 0.14 ± 0.15, 0.39 ± 0.25 and 2.66 ± 1.42) than in the RC+ group (0.04 ± 0.05, 0.29 ± 0.18, 0.08 ± 0.08, 0.29 ± 0.20 and 2.32 ± 1.00); Little to no difference was seen in DMFS (crown) between the 2 groups	No	Among healthy elderly individuals with root decay there may be an associated decrease in salivary function; These data are consistent with those of other studies reporting no significant relationship between diminished salivary flow and caries	General linear model analysis indicates that age, gender and salivary flow rates are not associated with the number of affected root surfaces; However, the mean number of active root caries lesions was low in the RC+ group
Zimmer et al.	1997	ND/NA	179 children, age 9-years-old, were re-examined 2 years after baseline	Germany; Participants whose 2-year caries increment exceeded a $D_{3,4}$MFS of 3 were considered as high risk	Out of the non-high risk group (n=135), 133 participants could be identified prospectively (specificity=98.5%, negative predictive value=76.9%); Out of the high risk group (n=44), only 4 participants could be correctly identified (sensitivity=9.1%, positive predictive value=66.7%)	No	Because of a poor sensitivity the parameters used in this clinical prospective study are only of low value to identify high caries risk children	No data presented on salivary buffer capacity as an individual measure of potential caries risk